

**REMARKS/ARGUMENTS**

Applicant notes with thanks the Examiner's determination that this application is eligible for continued examination under 37 C.F.R. § 1.114 and the Examiner's withdrawal of the finality of the previous Office Action. Applicant further notes with thanks the entry of the submission filed on February 25, 2004, including amendments to specification and to certain drawings and claims.

Applicant notes the request that a substitute statement regarding the biological deposit of *E. coli* NRRL B-30293 be filed with the correct date of deposit. Assurance is hereby given that the bacterial strain contained in Deposit Number NRRL B-30293 was deposited under the terms of the Budapest treaty on May 12, 2000. The deposits were made at the United States Department of Agriculture-Agriculture Research Service-National Center for Agriculture Utilization Research (USDA-ARS-NCAUR), 1815 North University Street, Peoria, Illinois 61604-3999, and given the accession number of NRRL B-30293. Assurance is also hereby given that the deposited bacterial strains are the same as the bacterial strains described in the specification and that the deposited bacterial strains were in the Applicant's possession at the time of filing (see attached deposit receipt). Finally, assurance is hereby given that all restrictions on the availability to the public of the deposited bacterial strains will be irrevocably removed upon the granting of a patent, subject to 37 C.F.R. § 1.808(b). Applicant submits that any amendment necessary to reflect the May 12, 2000, deposit date has been made previously, including in the amendment filed on February 25, 2004.

Claims 1, 2, 19, and 20 have been amended herein. Support for amendment to claim 1 is found in paragraphs [0015] and [0018], in original claim 1, and throughout the specification and

claims. Support for amendment to claim 2 is found in paragraphs [0025] and [0027], in original claim 2, and throughout the specification and claims. Support for the amendments to claims 19 and 20 is found in paragraphs [0044], [0050], and [0051], and throughout the specification and claims. Applicant respectfully submits that the amended claims add no new matter.

Claims 4 and 21 through 23 have been previously cancelled, and claims 9-11 and 14-18 have been previously withdrawn. Claims 24 through 31 are newly added herein. Support for claims 24 through 31 is found in paragraphs [0018], [0032], [0036], [0038], and throughout the specification and claims. Applicant respectfully submits that the newly added claims add no new matter to the Application.

Following entry of the amendment included herein, claims 1-3, 5-8, 12-13, 19-20, and 24-31 are pending in the application; claims 1, 2, 5-8, 12-13, and 19-20 stand rejected, claim 3 stands objected to, claims 24-31 are newly added and all claims are at issue. Applicant respectfully requests that all of the claims be allowed.

#### **Allowable Subject Matter**

The Non-Final Office Action includes an objection to claim 3 as being dependent upon a rejected base claim, but indicates that claim 3 would be allowable if rewritten in independent form including all of the limitations of the base claim (claim 2) and any intervening claims. Applicant submits that all rejections related to claim 2 have been traversed or otherwise rendered moot as discussed herein, and that claim 3 is therefore allowable as a dependent claim. Applicant respectfully requests that claim 3 be allowed.

#### **Objections to Drawings**

Applicant notes with thanks the acceptance of the corrected drawings of Figures 3A-3C and Figure 5, submitted February 25, 2004. In the Non-Final Office Action, The Examiner has

objected to the corrected drawing of Figure 4. Specifically, Figure 4 contains an inner box referring to "pyc ATCC 21253 IN E. coli" and "pyc NRRL B-11474 IN NRRL B-11474," and the Examiner questions what information other than that already contained in the legend of Figure 4 this box is supposed to convey. Applicant has amended Figure 4 to delete the inner box. Applicant believes that this amendment addresses the Examiner's objection, and Applicant respectfully requests that the drawing correction be approved.

### **Objections to Specification**

In the Non-Final Office Action, the Examiner has suggested that the description of Figure 2 be amended to refer to "*Corynebacterium glutamicum* ATCC 21253" and "*Corynebacterium glutamicum* NRRL B-11474" rather than "ATCC 21253" and "NRRL B-11474," respectively. Applicant has amended the specification accordingly. Accordingly, in view of the above and the amendment to the specification, Applicant respectfully submits that the Examiner's objections to the specification have been overcome and respectfully requests withdrawal of those objections.

The Examiner has also requested that, where necessary, the deposit date of *E. coli* NRRL B-30293 be amended to reflect the May 12, 2000 date of deposit. Applicant respectfully submits that such amendments were previously made in the response and amendment submitted on February 25, 2004, and asks that the objection be withdrawn.

### **§ 112 First Paragraph - Claims 1, 5-8 and 12-13**

The Office Action includes a rejection of pending claims 1, 5-8, 12, and 13 under 35 U.S.C. § 112, first paragraph, for alleged lack of an enabling disclosure. The Examiner has suggested that enablement should be shown in the specification by, for instance, demonstration of protein structural regions that may be modified without affecting pyruvate carboxylase activity, information regarding general tolerance of pyruvate carboxylase to such modification, a

scheme for modifying pyruvate carboxylase residues to obtain a desired function, and guidance regarding successful choices for modifications. Applicant submits that claim 1, as amended to include sequences with at least 95% homology to SEQ ID NO:1, satisfies the requirements of 35 U.S.C. § 112, first paragraph.<sup>1</sup>

As discussed in Applicant's response of August 22, 2003, and set forth in references incorporated in the specification and provided in the Information Disclosure Statement filed on August 19, 2002 (Modak, H.V. and Kelly, D.J., *Microbiology* 141:2619-2628 (1995), and Attwood, P.V., *Int. J. Biochem. Cell. Biol.* 27:231-249 (1995)), the structure of pyruvate carboxylase was known at the time that the invention was made.<sup>2</sup> Attwood, at Figure 10, page 242, sets forth an amino acid sequence of pyruvate carboxylase in yeast, including amino acid residues responsible for binding and activity of the enzyme. Attwood goes on to describe a region conserved between yeast pyruvate and transcarboxylase, as well as sequence homology among various biotin carboxylases at the N-terminus, the biotinyl domain, which corresponds to the mutation identified in SEQ ID NO:16. Furthermore, as was previously noted, none of the mutations suggested in claim 1 are located in the region characterized by Attwood as required for

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<sup>1</sup> Applicant would also like to respectfully direct the Examiner's attention to newly added claims 24 and 25, which include to subject matter identified in the Official Action as enabled by the disclosure. These claims are provided as part of Applicant's good-faith effort to advance prosecution of the Application. Their entry and allowance are respectfully requested.

<sup>2</sup> As set forth in the M.P.E.P., knowledge of those skilled in the art at the time the invention is made is relevant to enablement issues, whether or not the information is explicitly disclosed in the specification. "The specification need not disclose what is well-known to those skilled in the art and preferably omits that which is well-known to those skilled and already available to the public." M.P.E.P. § 2164.05(a).

pyruvate binding. Finally, Attwood reports two regions corresponding to SEQ ID NOS:6, 8, 10, 12, and 14, which correspond to a first partial reaction domain (ATP/HCO<sub>3</sub><sup>-</sup> binding) site having homology with acetyl Co-A carboxylase. Modak reports the inhibition of acetyl Co-A activation in the presence of aspartate.

Applicant submits that the requirements set forth by the Examiner have been satisfied. A region for pyruvate binding in a different species has been set forth, allowing one skilled in the art, with the benefit of the disclosure of the instant application, to make a conclusion regarding the tolerance of pyruvate carboxylase to modification and directing one away from modification of certain regions of the enzyme. Guidance regarding likely choices for successful modification and a scheme for modification are provided by the seven mutations listed in claim 1 and throughout the specification; use of one or more of these mutations in a sequence at least 95% similar to SEQ ID NO:1 provides a starting point for analysis, and the number of combinations of the seven mutations is not so great that an unreasonable amount of experimentation is necessary to successfully isolate a sequence of the invention.

Claims 5-8, 12, and 13, all of which depend from claim 1, are similarly enabled.

Applicant requests that the rejection be withdrawn and the claims allowed.

**§ 112 First Paragraph - Claims 19-20**

The Office Action includes a rejection of pending claims 19 and 20 under 35 U.S.C. § 112, first paragraph, for alleged lack of an enabling disclosure. Claims 19 and 20 have been amended herein. Applicant submits that claims 19 and 20, as amended, are enabled by the specification of the Application, and requests that the rejection be considered traversed and the claims allowed. Applicant states that SEQ ID NOS: 6, 8, 10, 12, 14, 16, and 18 represent conserved portions of SEQ ID NO:2, at positions 164-176, 193-205, 217-229, 238-250, 466-478,

1127-1139, and 1-18 of SEQ ID NO:2, respectively, and that satisfaction of claim 19 would include conservation of these sequences at similar relative locations in an amino acid sequence generated by a nucleotide sequence 95% identical to SEQ ID NO: 1.

**§ 112 Second Paragraph - Claims 1-3, 5-8, 12, and 13**

The Office Action includes a rejection of claims 1-3, 5-8, 12, and 13 under 35 U.S.C. § 112, second paragraph, for alleged indefiniteness related to function of the recited enzyme and mutation. Applicants submit that claims 1 and 2, as amended, are definite and that the rejection is traversed. Claims 3, 5-8, 12, and 13 depend either directly or indirectly from claims 1 and/or 2 and are similarly definite. Applicant requests that the rejection be withdrawn and the claims allowed.

**§ 102(a) - Claims 1, 5-8, 12, 13**

The Office Action includes a rejection of claims 1, 5-8, 12, and 13 as anticipated in light of Sinskey et al. (WO 00/39305, July 6, 2000, Genseq accession AAB01436). Claim 1, as amended, requires that the claimed enzyme be desensitized to feedback inhibition by aspartic acid. Sinskey does not include this limitation. Because Sinskey does not include all of the limitations of claim 1, claim 1 is patentable over Sinskey, and Sinskey is not a proper reference under 35 U.S.C. § 102(a). Because claim 1 is patentable over Sinskey and claims 5-8, 12, and 13 depend from claim 1, claims 5-8, 12, and 13 are also patentable over Sinskey. Applicant respectfully requests that the rejection be withdrawn and the claims allowed.

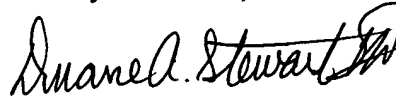
**Conclusion**

For at least the above-identified reasons, Applicant submits that claims 1-3, 5-8, 12-13 and 19-20 are in allowable form. Applicant believes the amendments made herein place the application in allowable form and respectfully requests entry of said amendments. Applicant

further submits that new claims 24-31 are in allowable form. Reconsideration of pending claims 1-3, 5-8, 12-13 and 19-20, allowance and passage to issue of those claims and of claims 24-31 are respectfully requested.

It is believed that this Amendment requires no fee above that included for the net addition of claims and for the two month extension of time. However, if an additional fee is required to make the response timely or otherwise valid, the Commissioner is hereby authorized to charge Deposit Account No. 02-4553 the necessary amount.

Respectfully submitted,



Dated: August 25, 2004

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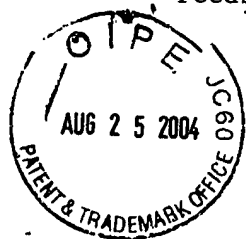
Attorneys for Applicant

**Amendments to the Drawings:**

The attached sheets of drawings include changes to Figure 4 as set forth in the Appendix. These sheets, which include Figure 4, replace the replacement sheet of the drawing for Figure 4, submitted with the Amendment dated February 25, 2004. In Figure 4, the inner box referring to "pyc ATCC 21253 IN E. coli" and "pyc NRRL B-11474 IN NRRL B-11474" has been deleted. Applicant submits that no new matter has been added by this deletion.

Attachment: Replacement Sheet (1)  
Annotated Sheet Showing Changes (1)





EFFECT OF ASPARTATE ON THE ACTIVITY OF PYRUVATE CARBOXYLASE  
FROM *C. glutamicum* NRRL B-11474 (○) AND ATCC 21253 (●).

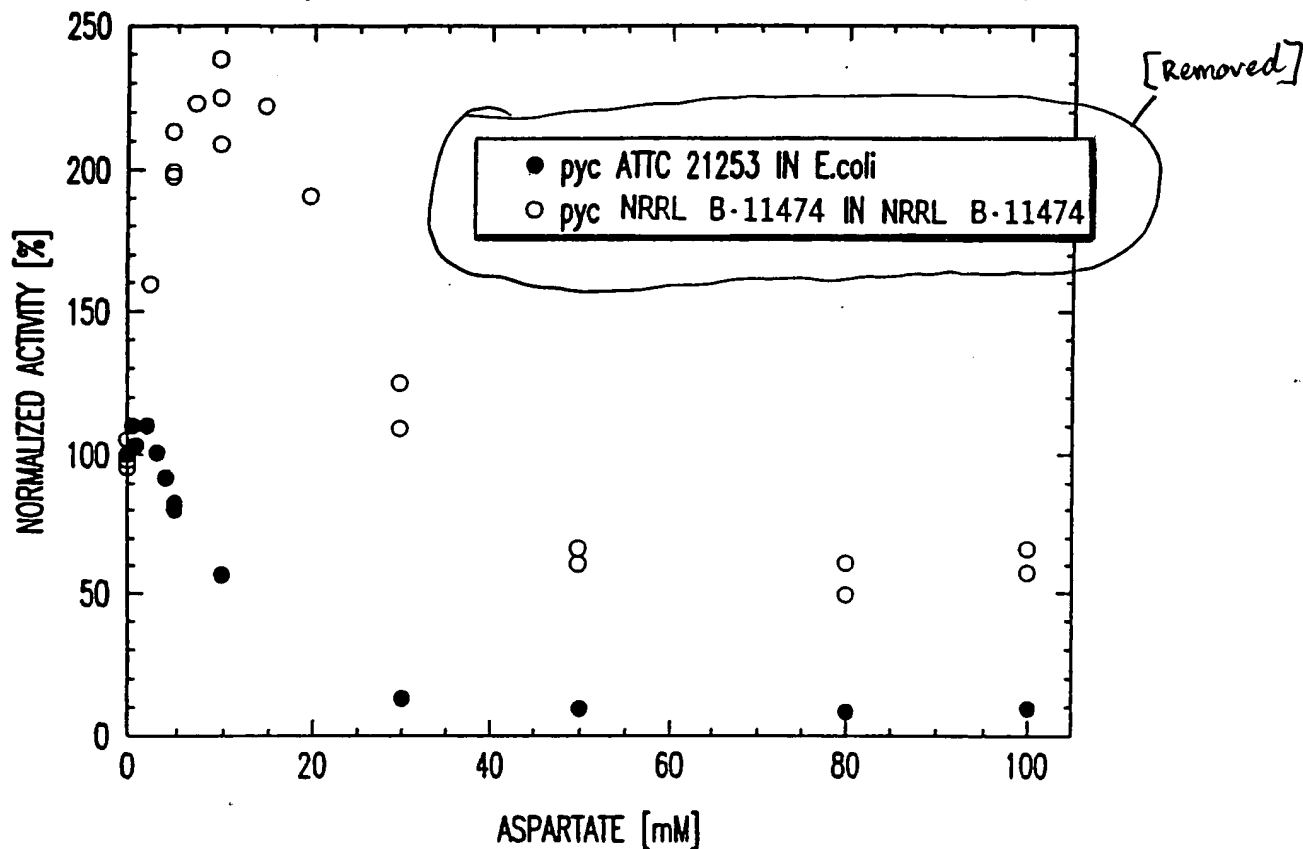


FIG. 4

## INTERNATIONAL FORM

TO

ADM

1001 N. Brush College Road  
Decatur, IL 62521

## VIABILITY STATEMENT

issued pursuant to Rule 10.2 by the  
INTERNATIONAL DEPOSITARY AUTHORITY  
identified at the bottom of this pageNAME AND ADDRESS OF THE PARTY TO WHOM  
THE VIABILITY STATEMENT IS ISSUED

<b>I. DEPOSITOR</b>  Name: ADM 1001 N. Brush College Road Address: Decatur, IL 62521	<b>II. IDENTIFICATION OF THE MICROORGANISM</b>  Depositor's taxonomic designation and accession number given by the INTERNATIONAL DEPOSITARY AUTHORITY: <i>Escherichia coli</i> NRRL B-30293  Date of: May 12, 2000 <input checked="" type="checkbox"/> <sup>2</sup> Original Deposit <input type="checkbox"/> <sup>2</sup> New Deposit <input type="checkbox"/> <sup>2</sup> Repropagation of Original Deposit
<b>III. (a) VIABILITY STATEMENT</b>  Deposit was found: <input checked="" type="checkbox"/> Viable <input type="checkbox"/> Nonviable on May 13, 2000 (Date) International Depositary Authority's preparation was found viable on May 29, 2000 (Date) <sup>3</sup>	
<b>III. (b) DEPOSITOR'S EQUIVALENCY DECLARATION</b>  Depositor determined the International Depositary Authority's preparation was <input checked="" type="checkbox"/> <sup>2</sup> Equivalent <input type="checkbox"/> <sup>2</sup> Not equivalent to deposit on <u>6/14/00</u> (Date) Signature of Depositor <u>[Signature]</u>	
<b>IV. CONDITIONS UNDER WHICH THE VIABILITY TEST WAS PERFORMED (Depositors/Depository)<sup>4</sup></b>  <u>LB broth supplemented with 100 ng/ml ampicillin</u>	
<b>V. INTERNATIONAL DEPOSITARY AUTHORITY</b>  Name: Agricultural Research Culture Collection (NRRL) International Depositary Authority  Address: 1815 N. University Street Peoria, Illinois 61604 U.S.A.	
Signature(s) of person(s) having the power to represent the International Depositary Authority or of authorized official(s): <u>[Signature]</u> Date: <u>6-1-00</u>	

<sup>1</sup> Indicate the date of the original deposit or when a new deposit has been made.<sup>2</sup> Mark with a cross the applicable box.<sup>3</sup> In the cases referred to in Rule 10.2(a)(ii) and (iii), refer to the most recent viability test.<sup>4</sup> Fill in if the information has been requested.